

REMARKS

Formal Matters

Claims 1-33 were pending in the application and were restricted into eight groups. Claims 1-11, 15, 19-30 and 32 are canceled. As discussed below, Applicants elect with traverse claims 12-14, 16-18, 31, and 33 (Group IV). Claims 12-14, 16, 31 and 33 are amended and claims 34-38 are added. No new matter is added by the amendments to the claims.

Support for the amendments is found throughout the specification such as at, for example, page 11, lines 23-25; page 11, line 27 to page 12, line 7; page 12, line 23 to page 13, line 2; page 13, lines 3-21; page 19, lines 22-23 (legend to Fig. 3) and Fig. 8; page 20, lines 17-22; page 22, line 15 to page 23, line 17; page 97, line 14 to page 98, line 7 and Fig. 4; and page 100, lines 5-10, Fig. 8, and Table 5 (page 100). No new matter is added by the amendments to the claims.

Sequence Rules

Applicants are required to comply with the sequence rules as set forth in 37 C.F.R. § 1.821-25 at the time of election of the restriction. Applicants believe that they have already complied with 37 C.F.R. § 1.821-25 by submitting a Letter and Request to Use Computer-Readable Sequence Listing Under 37 CFR § 1.821(e) upon filing the instant application on March 7, 2000 (copy of Letter enclosed). Specifically, the Letter requested that the computer-readable Sequence Listing filed in parent application Serial No. 09/070,416 be used as the computer-readable Sequence Listing for the instant application. A paper copy of the Sequence Listing and a statement that it is identical to the computer-readable copy from Serial No. 09/070,416 under 37 CFR § 1.821(e) was submitted with the Letter.

Applicants herewith submit another copy of the Sequence Listing for the convenience of the Examiner and in the unlikely circumstance that the

Examiner is unable to access the Sequence Listing filed in parent application Serial No. 09/070,416, Applicants request that the Examiner accept the Sequence Listing submitted herewith as the Sequence Listing for the instant application.

Applicants submit a copy of the Letter and Request and 37 CFR § 1.821(e), another paper copy of the Sequence Listing, and state that the computer readable copy and paper copy are identical, that no new matter is added by the amendment. As a result, Applicants believe that they have complied with the Notice to Comply.

Correction of Inadvertent Omission from the Specification When Filed

Upon filing the instant specification as a continuation of parent application 09/070,416 and provisional application serial no. 60/050,661, Appendix I was inadvertently omitted. Appendix I is a 15-page table comparing sequence identities between various light chain sequences. Insertion of the table into the specification does not add new matter because the table was present in the provisional application 60/050,661 to which the present application ultimately claims priority. Insertion of the Appendix as Table 6.1-6.15 is respectfully requested.

In a related application, U.S. application serial no. 08/850,058, the position of Appendix I was objected to. Appendix I was after "What is claimed is:" on page 103 and before the Claims. Applicants renamed the table as Table 6.1-6.15 and repositioned it to immediately before "What is claimed is:". Applicants respectfully offer this positioning scheme for consideration in the instant application.

Applicants submit Table 6.1-6.15 on fifteen pages. The word "Appendix" and the original page number on each page of the original appendix are deleted and "Table 6.X" is inserted therefor, where "X" refers to subpart 1-15 of Table 6.

The word "Appendix" occurs only once in the originally filed specification at page 96, line 24. The word "Appendix" has been deleted from the specification and the term "Table 6.1-6.15" has been inserted therefor.

No new matter has been added by these amendments to the

Other Amendments to the Specification

Applicants amended the specification on page 13, line 27 to correct a typographical error by replacing a semicolon (";") with a period ("."). No new matter was added by the amendment to the specification.

Applicants amended the specification to correct a typographical error in the legend for Fig. 2A-2C on page 17, line 30. Specifically, Fig. 2C shows the sequence of a portion of the nucleic acid construct depicted in Fig. 2E. Originally filed Fig. 2C indicates that that sequence is SEQ ID NO:13 and thus provides support for the amendment. Correction of the legend for Fig. 2C has been corrected accordingly. No new matter has been added by the amendment to the specification.

Election/Restriction

The Examiner has indicated that the application contains claims directed to patentably distinct species of the claimed invention and requires restriction under 35 U.S.C. § 121 according to the eight groupings indicated in the Office Action (Paper No. 4, mailed July 5, 2001)

In addition, Applicants were asked to further elect patentably distinct species of the claimed invention as indicated on page 4 of the Office Action. Applicants elect with traverse, for the reasons stated herein, the following species:

The constant domain is from a human IgG.

The anti-Ob-R/anti-HER3 species.

Applicant respectfully traverses the restriction and election requirement as applied to the currently pending claims for the reasons provided below.

Applicant respectfully traverses the restriction requirement in which free thiol or protuberance/cavity structures within the polypeptide sequence are relied upon to support the restriction. The

Applicant respectfully traverses the restriction requirement in which the presence of a specific amino acid sequence is relied upon to support the restriction. The

class 530 and subclass 387.3 as another multispecific antibody of the invention comprising a protuberance and cavity in the multimerization domain (Group IV). Thus, the Examiner would not be placed under an undue burden to search in the same class and subclass of art in order to evaluate the patentability of claims in Groups III and IV, for example. The same argument applies to Groups I and II, Groups V and VI, and Groups VII and VIII. Applicants respectfully submit that the restrictions that distinguish Group I from Group II, Group III from Group IV, Group V from Group IV, and Group IV from Group VIII should be withdrawn.

Without acquiescing to the restrictions, however, and merely to expedite prosecution of the claims, Applicants elect with traverse Group IV, Claims 12-14, 16-18, 31 and 33 drawn to a multispecific antibody, wherein the multimerization domain is altered to comprise a protuberance and a cavity.

With respect to the election of species requirement, Applicants respectfully traverse the election requirement for failing to recognize Applicant's right to allowed claims that link a reasonable number of species under 37 CFR § 1.141. It is Applicant's understanding and right under 37 CFR § 1.141 that, following election, the claims will be examined fully with respect to the elected species and further to the extent necessary to determine patentability for a reasonable number of species encompassed by the generic claims.

With the above reservation of right, Applicant elects, with traverse, a constant domain from a human IgG and further elects anti-Ob-R/anti-HER3, an illustrative example of the claimed multispecific antibody of the invention.

A marked-up version and a clean version of the pending claims is attached.

If the Examiner has any questions, the Examiner should feel free to call the undersigned attorney at the number indicated below.

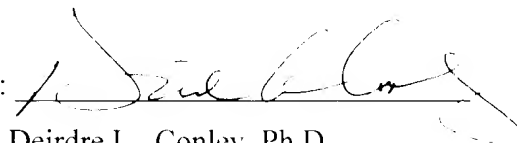
This document is timely filed with a petition and fees for a three-month extension of time. In the unlikely event that additional fees are due, Applicants hereby petition the Commissioner to authorize any extensions of time and/or to deduct fees from or add credits to our Deposit Account 07-0630 as necessary to maintain the pendency of this application.

Respectfully submitted,

GENENTECH, INC.

Date: November 5, 2001

By:



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PATENT TRADEMARK OFFICE

Doc. #99911

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Deleted information is shown in strikethrough (~~Θ~~), and added information is shown as underlined.

Paragraph beginning at page 13, line 26, has been amended as follows:

(ii) recovering the multispecific antibody from the host cell culture;;

Paragraph beginning at page 17, line 16, has been amended as follows:

Figs. 2A-2C. Fig. 2A diagrams a selection scheme for C₃ heterodimer using phage display vector, pFA2. Phage displaying stable C₃ heterodimers are captured using an antibody directed to the gD flag. Fig. 2B diagrams a dicistronic operon in which C₃ expressed from a synthetic gene is co-secreted with a second copy of C₃ expressed from the natural gene (Ellison et al. Nucleic Acids Res. 10:4071-4079 (1982)) as a fusion protein with M13 gene III protein. The synthetic C₃ gene is preceded by a sequence encoding a peptide derived from herpes simplex virus glycoprotein D (gD flag, Lasky, L. A. and Dowbenko, D. J. (1984) DNA 3:23-28; Berman, P. W. et al., (1985) Science 227:1490-1492 and a cleavage (G) site for the site-specific protease, Genenase I (Carter, J. et al. (1989) Proteins: Structure, Function and Genetics 6:240-248). Fig. 2C is the nucleic acid sequence of the dicistronic operon (~~SEQ ID NO:1~~) (SEQ ID NO: 13) of Fig. 2B in which the residues in the translated C₃ genes are numbered according to the

gene (366, 368, and 407).

Paragraph beginning at page 96, line 8, has been amended as follows:

--A large human single chain Fv (scFv) antibody library (Vaughan *et al.* (1996), *supra*) was panned for antibodies specific for eleven antigens including Axl(human receptor tyrosine kinase ECD), G-CSF-R (human granulocyte colony stimulating factor receptor ECD), IgE (murine IgE), IgE-R (human IgE receptor α -chain), MPL (human thrombopoietin receptor tyrosine kinase ECD), MusK (human muscle specific receptor tyrosine kinase ECD), NpoR (human orphan receptor NpoR ECD), Ese (human receptor tyrosine kinase, Ese, ECD), HER3 (human receptor tyrosine kinase HGF3/c-erbB3 ECD), Ob-R (human leptin receptor ECD), and VEGF (human vascular endothelial growth factor) where ECD refers to the extracellular domain. The nucleotide sequence data for scFv fragments from populations of antibodies raised to each antigen was translated to derive corresponding protein sequences. The V_H sequences were then compared using the program "align" with the algorithm of Feng and Doolittle (1985, 1987, 1990) to calculate the percentage identity between all pairwise combinations of chains (Feng, D.F. and Doolittle, R.F. (1985) *J. Mol. Evol.* 21:112-123; Feng, D.F. and Doolittle, R.F. (1987) *J. Mol. Evol.* 25:351-360; and Feng, D.F. and Doolittle, R.F. (1990) *Methods Enzymol.* 183:375-387). The percent sequence identity results of each pairwise light chain amino acid sequence comparison were arranged in matrix format (~~Appendix~~ Table 6.1-6.15).

The Appendix is amended to become Table 6.1-6.15 as follows:

[illegible]

[illegible]

APPENDIX

A

Table
6.6

	MusK				NpoR				Rse													
	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73
52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74
79	80	79	81	81	44	45	45	80	46	46	46	48	72	81	49	46	47	47	45	81	49	50
47	47	47	48	50	59	46	45	47	73	73	71	70	42	48	71	69	71	70	70	48	71	72
48	48	48	49	51	61	47	46	48	75	75	73	72	43	49	73	71	73	71	72	49	73	74
83	84	83	100	81	44	48	46	84	47	47	46	45	88	100	46	43	47	44	45	100	46	75
77	78	77	82	79	48	48	47	78	49	49	51	51	80	82	52	48	52	50	50	82	52	83
98	99	98	83	76	43	46	44	99	47	47	47	46	73	83	47	43	48	45	46	83	47	84
78	79	78	83	80	48	48	46	79	49	49	51	51	74	83	52	48	52	50	50	83	52	85
48	48	48	48	49	58	44	44	48	80	80	65	63	41	48	64	60	67	62	64	48	64	86
48	48	48	49	51	63	46	48	48	75	75	66	65	42	49	66	61	66	64	65	49	66	87
47	47	47	46	49	61	48	47	47	66	66	89	99	41	46	100	95	90	98	88	46	100	88
85	85	85	85	81	45	46	46	85	48	48	47	47	77	85	48	45	48	46	46	85	48	89
47	47	47	45	47	62	45	46	47	62	62	80	84	40	45	85	84	81	83	79	45	85	90
99	100	99	84	77	43	46	44	100	47	47	47	46	74	84	47	43	48	45	46	84	47	91
44	44	44	44	46	58	46	45	44	61	61	84	94	40	44	95	90	86	93	86	44	95	92
47	47	47	48	50	62	50	49	47	65	65	88	89	42	48	90	86	89	88	88	48	90	93
41	42	41	42	44	98	47	46	42	57	58	58	38	42	59	52	52	59	57	57	42	59	94
41	42	41	42	43	91	48	49	42	57	58	57	57	38	42	58	52	58	57	57	42	58	95
42	43	42	44	46	100	49	48	43	59	60	60	60	40	44	61	54	61	59	59	44	61	96
47	47	47	46	49	61	48	47	47	66	66	89	99	41	46	100	95	90	98	88	46	100	97
48	48	48	49	51	60	46	45	48	75	74	72	71	43	49	72	71	72	70	72	49	72	98
48	48	48	49	51	61	47	46	48	75	75	73	72	43	49	73	71	73	71	72	49	73	99
81	82	81	98	79	43	47	45	82	46	46	45	44	86	98	45	42	46	43	44	98	45	100
49	49	49	48	51	61	49	49	49	70	70	89	93	43	48	94	89	90	92	88	48	94	101
42	43	42	44	46	100	49	48	43	59	60	60	60	40	44	61	54	61	59	59	44	61	102
98	99	98	84	77	43	46	44	99	47	47	47	46	74	84	47	43	48	45	46	84	47	103
42	43	42	44	46	100	49	48	43	59	60	60	60	40	44	61	54	61	59	59	44	61	104
48	48	48	46	50	61	48	45	48	60	60	74	80	40	46	80	79	75	79	73	46	80	105
42	43	42	44	46	99	49	48	43	58	59	59	59	40	44	60	53	60	58	58	44	60	106
47	47	47	46	49	61	48	47	47	66	66	89	99	41	46	100	95	90	98	88	46	100	107
44	45	44	46	48	99	48	47	45	59	59	59	59	40	46	60	54	60	58	59	46	60	108
42	43	42	42	44	88	48	49	43	57	57	56	56	36	42	57	52	57	55	56	42	57	109
43	44	43	45	47	100	47	47	44	58	58	58	58	41	45	59	54	59	57	58	45	59	110
98	99	98	83	76	43	46	44	99	47	47	47	46	74	83	47	43	48	45	46	83	47	111
47	47	47	48	50	72	48	45	47	63	63	73	78	42	48	79	78	74	77	73	48	79	112
79	80	79	81	81	45	46	46	80	47	47	47	49	49	73	81	50	46	48	46	81	50	113
48	48	48	50	52	67	47	45	48	73	73	65	65	47	50	66	64	66	64	65	50	66	114
47	47	47	46	52	59	46	43	47	64	64	75	83	41	46	84	83	76	82	74	46	84	115
94	95	94	83	75	44	47	45	95	47	47	48	47	74	83	48	43	49	46	47	83	48	116
95	96	95	80	73	40	43	43	96	43	43	43	42	72	80	43	43	44	43	44	80	43	117
83	84	83	100	81	44	48	46	84	47	47	46	45	88	100	46	43	47	44	45	100	46	118

[illegible]

1965
6.00

[illegible]

80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107
45	81	100	85	51	47	80	48	85	46	44	85	46	79	82	48	46	79	100	100	100	100	79	100	46	50	78	80
72	48	49	51	92	65	47	74	51	73	59	51	73	47	49	75	73	47	49	49	49	47	47	49	73	98	46	47
74	49	50	52	94	67	48	76	52	75	61	52	75	48	50	77	75	48	50	50	50	48	48	50	75	100	47	48
46	100	81	85	49	45	84	46	85	47	44	85	47	84	83	45	47	83	81	81	81	83	77	81	47	49	82	84
48	82	83	83	54	51	78	50	83	49	48	83	49	78	83	51	49	78	83	83	83	77	77	83	49	53	76	78
46	83	79	85	49	47	99	46	85	47	43	85	47	98	94	45	47	98	79	79	79	97	97	79	47	48	96	99
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80	48	46	49	75	61	48	70	49	80	58	49	80	48	48	66	80	49	46	46	46	48	48	46	80	72	47	48
74	49	49	50	80	63	48	86	50	75	63	50	75	48	50	67	75	48	49	49	49	47	47	49	75	79	47	48
65	46	49	49	76	80	47	62	49	66	61	49	66	47	49	92	66	47	49	49	49	47	47	49	66	73	46	47
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70	48	49	51	76	74	49	63	51	70	61	51	70	49	50	87	70	49	49	49	49	49	49	49	70	73	48	49
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42	80	78	83	45	43	96	44	83	43	40	83	43	95	91	42	43	95	78	78	78	94	94	78	43	44	93	96
46	100	81	85	49	45	84	46	85	47	44	85	47	84	83	45	47	83	81	81	81	83	83	81	47	49	82	84

				-	53	48	86	47	100	50	45	100	50	87	85	49	50	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85
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44	46	84	83	83	44	49	46	83	84	41	Mpl.16
62	82	48	46	46	62	65	83	49	48	42	Mpl.19
43	47	86	100	100	43	46	47	85	86	43	Mpl.21
44	48	86	100	100	44	48	48	85	86	44	Mpl.24
61	96	50	48	48	61	69	97	51	50	45	Mpl.26
44	46	84	83	83	44	48	46	82	84	46	Mpl.28
54	61	44	43	43	54	94	61	47	44	47	Mpl.29
59	65	49	46	46	59	78	65	50	49	48	Mpl.30
60	66	50	47	47	60	79	66	51	50	49	Mpl.31
61	65	46	45	45	61	99	65	48	46	50	Mpl.32
57	78	47	46	46	57	60	79	49	47	51	Mpl.33
42	47	85	99	99	42	46	47	84	85	52	Mpl.35
43	47	86	100	100	43	46	47	85	86	53	Musk.01
42	47	85	99	99	42	46	47	84	85	54	Musk.02
44	46	85	84	84	44	48	46	83	85	55	Musk.06
46	49	80	77	77	46	50	49	78	80	56	NpoR.25
100	60	45	43	43	99	61	61	46	45	57	NpoR.44
49	48	48	46	46	49	45	48	49	48	58	NpoR.53
48	47	46	44	44	48	46	47	48	46	59	NpoR.81
43	47	86	100	100	43	46	47	85	86	60	NpoR.86
59	66	50	47	47	59	78	66	51	50	61	Rse.01
60	66	50	47	47	60	79	66	51	50	62	Rse.02
60	88	48	47	47	60	65	89	49	48	63	Rse.03
60	98	48	46	46	60	65	99	49	48	64	Rse.04
40	41	75	74	74	40	44	41	80	75	65	Rse.07
44	46	85	84	84	44	48	46	83	85	66	Rse.08
61	99	49	47	47	61	66	100	50	49	67	Rse.15
54	94	45	43	43	54	62	95	46	45	68	Rse.16
61	90	49	48	48	61	66	90	50	49	69	Rse.18
59	97	47	45	45	59	64	98	48	47	70	Rse.20
59	88	47	46	46	59	65	88	48	47	71	Rse.21
44	46	85	84	84	44	48	46	83	85	72	Rse.22
61	99	49	47	47	61	66	100	50	49	73	Rse.23
43	45	84	83	83	43	48	45	83	84	74	Rse.24
64	82	51	49	49	63	70	83	52	51	75	Rse.52
59	72	52	48	48	59	73	73	53	52	76	Rse.53
100	60	45	43	43	99	61	61	46	45	77	Rse.58
60	66	50	47	47	60	79	66	51	50	78	Rse.60
44	49	85	80	80	44	48	49	85	85	79	Rse.61
59	65	49	46	46	59	78	65	50	49	80	Rse.63
44	46	85	84	84	44	48	46	83	85	81	her3.1
44	49	85	80	80	44	48	49	85	85	82	her3.10

45	49	100	86	86	45	47	49	99	100	83	her3.11
65	75	53	49	49	64	73	76	54	53	84	her3.12
60	79	48	47	47	60	61	80	49	48	85	her3.16
43	47	86	100	100	43	46	47	85	86	86	her3.18
61	62	47	46	46	60	75	62	49	47	87	her3.19
45	49	100	86	86	45	47	49	99	100	88	her3.22
60	66	50	47	47	60	79	66	51	50	89	her3.3
100	60	45	43	43	99	61	61	46	45	90	her3.4
45	49	100	86	86	45	47	49	99	100	91	her3.7
60	66	50	47	47	60	79	66	51	50	92	obr.1
43	47	87	99	99	43	46	47	86	87	93	obr.11
44	49	85	95	95	44	48	49	83	85	94	obr.12
63	91	49	45	45	63	66	92	51	49	95	obr.14
60	66	50	47	47	60	79	66	51	50	96	obr.15
43	47	85	99	99	43	46	47	84	85	97	obr.16
44	49	85	80	80	44	48	49	85	85	98	obr.17
44	49	85	80	80	44	48	49	85	85	99	obr.18
44	49	85	80	80	44	48	49	85	85	100	obr.19
43	47	85	98	98	43	46	47	83	85	101	obr.2
43	47	86	99	99	43	46	47	85	86	102	obr.20
44	49	85	80	80	44	48	49	85	85	103	obr.21
60	66	50	47	47	60	79	66	51	50	104	obr.22
61	72	52	48	48	60	71	73	53	52	105	obr.23
42	46	85	97	97	42	45	46	83	85	106	obr.24
43	47	86	100	100	43	46	47	85	86	107	obr.26
-	60	45	43	43	99	61	61	46	45	108	obr.3
-	49	47	47	47	60	66	99	50	49	109	obr.4
	-	86	86	45	47	49	99	100	110	veg1.1	
		-	100	43	46	47	85	86	111	veg1.10	
			-	43	46	47	85	86	112	veg1.2	
				-	61	61	46	45	113	veg1.3	
					-	66	49	47	114	veg1.4	
						-	50	49	115	veg1.5	
							-	99	116	veg1.6	
									117	veg1.8	
108	109	110	111	112	113	114	115	116	117		Clone
					VEGF						

In the Claims:

Claims 1-11, 15, 19-30 and 32 have been cancelled.

Claims 34-38 have been added.

Claims 12-14, 16, 31, and 33 have been amended as follows:

12. (Amended) A multispecific antibody prepared by the method
[of claim 1] comprising:

(a) expressing in a host cell a first polypeptide comprising a first heavy chain variable domain, a first or second light chain variable domain, and a first multimerization domain, wherein the first and second light chain variable domains have at least 80% amino acid sequence identity, and wherein a first binding domain is formed by the first heavy chain variable domain and the first or second light chain variable domain;

(b) expressing in the host cell a second polypeptide comprising a second heavy chain variable domain, the first or the second light chain variable domain, and a second multimerization domain, wherein a second binding domain is formed by the second heavy chain variable domain and the first or second light chain variable domain, and wherein the first and second binding domains bind different antigens;

(c) allowing the first and second polypeptides to dimerize by interaction of the first and second multimerization domains to form a multispecific antibody; and

(d) recovering the multispecific antibody from the host cell.

13. (Amended) A multispecific antibody comprising a first polypeptide and at least one additional polypeptide [which meet at an interface, wherein], the multispecific antibody comprising:

[(a) the first polypeptide comprises a multimerization domain

and a first heavy chain variable domain, a first or second light chain variable domain, wherein the variable light chain of the first and

34. (New) The multispecific antibody of claim 13, wherein the first and second light chain variable domains have at least 90% amino acid sequence identity.

35. (New) The multispecific antibody of claim 13, wherein the first and second light chain variable domains have at least 95% amino acid sequence identity.

36. (New) The multispecific antibody of claim 13, wherein the first and second light chain variable domains have at least 98% amino acid sequence identity.

37. (New) The multispecific antibody of claim 13, wherein the first and second light chain variable domains have at least 99% amino acid sequence identity.

38. (New) The multispecific antibody of claim 13, wherein the first and second light chain variable domains have identical amino acid sequences.